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(71)Applicant : GOGAKU REISHI HONPO:KK

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(72)Inventor : SASAKI HIROYUKI
ITO HIROKO
SHIMURA KEISHIRO
ITO HITOSHI

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(54) ANTI-CANCER MEDICINE, MACROPHAGE ACTIVITY IMPARTER AND FUNCTIONAL FOOD

(57)Abstract:

PROBLEM TO BE SOLVED: To obtain an anti-cancer medicine and a macrophage activity imparter having excellent anti-cancer action and macrophage activity action by making the imparter include a composition composed of an *Agaricus blazei* Mycelial extract and an extracting of fruit body of *Ganoderma lucidum* as an active ingredient.

SOLUTION: This imparter comprises a composition composed of (A) an *Agaricus blazei* Mycelial extract and (B) an extract of fruit body of *Ganoderma lucidum* and preferably further (C) royal jelly as an active ingredient. For example, the amounts of the components mixed are 10-90 wt.% of the component A, 1-60 wt.% of the component B and 0-50 wt.% of the component C. Preferably 100-10,000 mg of an anti-cancer medicine having the mixed ratio is orally administered daily once or several times dividedly. The component A and the component B are obtained by properly grinding the mycelium of *Agricus blazei* Murrill and fruit body of *Ganoderma lucidum*, extraction-treating them with water, methanol, etc., appropriately filtering, concentrating, etc.

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- 2.**** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention]This invention relates to the functional food containing the anticancer agent which makes an active principle the mycelium extract of *Agaricus blazei*, a *Ganoderma* extract, etc., a macrophage activity grant agent, and the extract concerned.

[0002]

[Description of the Prior Art]Cancer is an illness always located in the higher rank of an adult cause of death.

Many researchers are doing their best in discovery of an effective specific.

[0003]By the way, *Agaricus blazei* by which this invention persons belonged to the *Agaricus* and artificial cultivation was carried out at the Iwade mycology research institute () [*Agaricus blazei* Murrill and] It found out that the mycelium extract (*Agaricus blazei* Mycelial extract) produced by cultivating 101 shares of Iwade had anticancer activity, and it was already reported (Anticancer Res.17:227-284 (1997)). It is one sort of the medicinal mushroom belonging to Polyporaceae (Polyporaceae), It found out that had sthenia, blood supplement, moral stability, irrigation, a **** operation, etc., and *Ganoderma* (*Ganoderma lucidum*) validated with illnesses, such as a cough, bronchitis, and arthritis, had an anticancer operation, and it was already reported (Mie. Med. J.26:147-152 (1977)). Royal jelly is also called royal jelly and royal jelly, and contains various vitamin groups, acetylcholine, 10-hydroxy 2-decenoic acid with an anticancer operation, etc.

[0004]

[Problem(s) to be Solved by the Invention]However, what should not necessarily be satisfied could not say those anticancer operations, and their macrophage activity was also low.

[0005]Therefore, an object of this invention is to provide drugs excellent in the anticancer operation or the macrophage active work, and functional food.

[0006]

[Means for Solving the Problem]If royal jelly is further used together with concomitant use or these for a mycelium extract and a *Ganoderma* extract of above-mentioned *Agaricus blazei* as a result of inquiring wholeheartedly that this invention persons should attain the above-mentioned purpose, It

compared, when they were used independently, and it found out that a remarkable anticancer operation and a macrophage active work were obtained especially, and this invention was completed.

[0007] That is, this invention provides an anticancer agent which makes an active principle a constituent which consists of a mycelium extract and a Ganoderma extract of *Agaricus blazei*. This invention provides an anticancer agent which makes an active principle a constituent which consists of a mycelium extract, a Ganoderma extract, and royal jelly of *Agaricus blazei* again. This invention provides a macrophage activity grant agent which makes an active principle a constituent which consists of a mycelium extract and a Ganoderma extract of *Agaricus blazei* again. This invention provides a macrophage activity grant agent which makes an active principle a constituent which consists of a mycelium extract, a Ganoderma extract, and royal jelly of *Agaricus blazei* again. This invention provides functional food which contains again a constituent which consists of a mycelium extract and a Ganoderma extract of *Agaricus blazei*. This invention provides functional food which contains again a constituent which consists of a mycelium extract, a Ganoderma extract, and royal jelly of *Agaricus blazei*.

[0008]

[Embodiment of the Invention] Although any of a natural product and an artificial culture thing may be sufficient as *Agaricus blazei*, its artificial culture thing is preferred. *Agaricus blazei* uses a mycelium. Arbitrary parts, such as ****, a stipe, and a mycelium, or the whole can be used for Ganoderma. The mycelium extract and Ganoderma extract of *Agaricus blazei*, After grinding the mycelium concerned and Ganoderma suitably, it can obtain by these mixtures' extracting, and filtering and condensing suitably, hydrocarbon, such as ketone, such as alcohols, such as water, methanol, and ethanol, and acetone, and cyclohexane. According to this method, an about 80-100-mg extract is usually obtained from 100g (about 90% of moisture) of myceliums of fresh *Agaricus blazei* as solid content, and an about 500-600-mg extract is obtained from 100g (about 14 to 16% of moisture) of dry Ganoderma as solid content. Further, by a chromatography etc., what carried out fractionation, for example to the fraction with a specific polysaccharide fraction etc. may be sufficient as these extracts, and they may use a commercial item. Although a liquid, paste state, and the gestalt of powdered ***** may be sufficient as royal jelly, its shape of powder is preferred, and a commercial item may be used for it.

[0009] The anticancer agent, the macrophage activity grant agent, and functional food of this invention, The above-mentioned *Agaricus blazei* mycelium extract, a Ganoderma extract, and the ingredient generally further used for royal jelly, other anticancer agents, etc. if needed are mixed, and it can manufacture by using arbitrary gestalten, such as an emulsion, suspension, paste state, powder, and a solid state.

[0010] The dosage form of the anticancer agent of this invention and a macrophage activity grant agent has preferred internal use, although which gestalt may be sufficient as internal use, injection administration, dermal administration, etc. When administering orally, the loadings of the mycelium extract of *Agaricus blazei* in an anticancer agent or macrophage activity grant agent, a Ganoderma extract, and royal jelly are as follows. As for especially the mycelium extract of *Agaricus blazei*, 20 to 80 % of the weight is preferred ten to 90% of the weight, as for especially a Ganoderma extract, 10 to 50 % of the weight is preferred one to 60% of the weight, and 0 to 50 % of the weight of royal jelly is

preferred. The loadings of the mycelium extract of *Agaricus blazei* in the functional food of this invention, a *Ganoderma* extract, and royal jelly are as follows in solid content conversion. As for especially the mycelium extract of *Agaricus blazei*, 10 to 90 % of the weight is preferred one to 99% of the weight, as for especially a *Ganoderma* extract, 10 to 90 % of the weight is preferred one to 99% of the weight, and 0 to 90 % of the weight of royal jelly is preferred. It is preferred to carry out the 1,000-2,000-mg ingestion of 100-10,000 mg of the anticancer agent, the macrophage activity grant agent, or functional food of this blending ratio especially in 1 time or several steps on the 1st.

[0011]

[Example]Next, although an example is shown and this invention is explained still in detail, this invention is not limited to the following examples.

[0012]Using hot water, the cultured mycelium of reference example 1 *Agaricus blazei* (101 shares of lwade) was extracted for 3 hours, was filtered and condensed at 100 **, and the extraction extract (henceforth "ABME") of 18 % of the weight of solid content was obtained.

[0013]75 % of the weight and a 5 mountain *Ganoderma* Original house] and 96 % of the weight of solid content: "GLE") were mixed for the example 1 above-mentioned ABME 25% of the weight, and the constituent 1 (an anticancer agent, a macrophage activity grant agent, functional food) was obtained.

[0014]The example 2 above-mentioned ABME was mixed 60% of the weight, 20 % of the weight and the end of royal jelly (it is called below KOHKAN make and 25 % of the weight of solid content: "RJ") were mixed for the above GLE 20% of the weight, and the constituent 2 (an anticancer agent, a macrophage activity grant agent, functional food) was obtained.

[0015]Example of examination 1 One groups [eight] divided 48 ICR/Sic system feminity mice of 5 weeks old of anticancer activity of the constituent concerning this invention into each six groups. The Sacroma180 cancer cell (5×10^6 individual) extracted from the mouse on the 7th after transplantation was transplanted to the 1st group - the 5th group. Subsequently, the class product obtained 24 hours after in Examples 1 and 2 was administered orally to the 1st group - the 4th group with the stomach tube for 20 days 1 time respectively every morning and evening on the conditions shown in Table 1. The 5th group was medicated with the physiological saline instead of the constituent concerned, a cancer cell was not transplanted to the 6th group, and only the physiological saline was prescribed for the patient. The cancer part was extracted from each group 21 days after carcinomatous implants, and the balancer product, the cancer control rate, cancer perfect disappearance rate, and survival rate of the cancer part were measured. The measuring method is as follows. The volume (cm^3) of cancer is expressed with $2\pi a^2 b \times 10^{-3} / 3$ (however, a shows the minor axis (mm) of cancer and b shows the major axis (mm) of cancer). A cancer control rate (%) is expressed with $x(1 - (\text{traveler's check}))$ 100 (however, T shows the volume of the cancer of the above-mentioned constituent administration group, and C shows the balancer product of the cancer of the 5th group). The cancer perfect disappearance rate was expressed with the rate of the mouse that cancer disappeared thoroughly. The survival rate was expressed with the rate of the mouse of having survived. A result is shown in Table 1.

[0016]

[Table 1]

試験群	投与物	1回の投与量	ガン体積 (cm ³)	ガン抑制率 (%)	ガン完全消失率	生存率
第1群	組成物1	250mg/kg	6.3±2.7	75.5	2/8	7/8
第2群	組成物1	500mg/kg	3.2±1.9	87.6	4/8	8/8
第3群	組成物2	250mg/kg	9.5±2.8	63.0	2/8	6/8
第4群	組成物2	500mg/kg	6.0±1.3	76.7	3/8	8/8
第5群	—	—	25.7±5.5	0	0/8	3/8
第6群	—	—	—	—	—	8/8

[0017]The cancer of 25 to 50% of mouse disappeared thoroughly both the 1st group - the 4th group. Especially, by the 2nd group, a cancer control rate is 87.6%, a perfect disappearance rate is 50%, and remarkable anticancer activity was accepted.

[0018]One groups [ten] divided 60 ICR/Slc system feminity mice of 5 weeks old of anticancer activity of example of examination 2 GLE, or ABME into each six groups. The Sacroma180 cancer cell (5x10⁶ individual) extracted from the mouse on the 7th after transplantation was transplanted to the 7th group - the 11th group. Subsequently, said GLE or ABME was administered orally to the 7th group - the 10th group with the stomach tube for 20 days 1 time respectively every morning and evening on the conditions shown in Table 2, respectively 24 hours after. The 11th group was medicated with the physiological saline instead of GLE concerned and ABME, a cancer cell was not transplanted to the 12th group, and only the physiological saline was prescribed for the patient. The balancer product of the cancer of each group and the cancer control rate were measured 21 days after carcinomatous implants. The cancer perfect disappearance rate and the survival rate were measured on the 28th. The measuring method is the same as that of the example 1 of an examination. A result is shown in Table 2.

[0019]

[Table 2]

試験群	投与物	1回の投与量	ガン体積 (cm ³)	ガン抑制率 (%)	ガン完全消失率	生存率
第7群	GLE	62.5mg/kg	15.6±3.1	19.2	0/10	4/10
第8群	GLE	125mg/kg	11.7±4.2	39.4	2/10	5/10
第9群	ABME	187.5mg/kg	10.4±3.9	46.1	3/10	6/10
第10群	ABME	375mg/kg	7.3±3.0	62.2	3/10	8/10
第11群	—	—	19.3±2.9	0	0/10	2/10
第12群	—	—	—	—	—	10/10

[0020]The cancer control rate was inferior to the 1st group - the 4th group in both the 7th group - the 10th group. The cancer perfect disappearance rate was inferior to the 1st group, the 2nd group, and the 4th group in the 7th group, the 8th group, and the 10th group. The combined effect of GLE, ABME, and RJ was checked from the examples 1 and 2 of an examination.

[0021]Example of examination 3 One groups [five] divided the 30 same mice as the example 1 of the macrophage activity grant effect examination of the constituent concerning this invention into

each six groups, the cancer cell was transplanted like [group / 5th] the example 1 of an examination from the 1st group, and administration of the class product or the physiological saline was performed. A cancer cell was not transplanted to the 6th group, and only the physiological saline was prescribed for the patient. The peritoneal macrophage of the mouse of each group was collected 24 hours after the last administration, and the number of macrophages was measured by the method of the method (Antitumor Res. 15:1937-1948 (1995)) of Ito and others. Subsequently, the rate (% and macrophage activity 1) of the number of macrophages of each group to the number of macrophages of the 5th group and the rate (% and macrophage activity 2) of the number of macrophages of each group to the number of macrophages of the 6th group were computed. A result is shown in Table 3.

[0022]

[Table 3]

試験群	投与物	1回の投与量	マクロファージ数 ($\times 10^6$)	マクロファージ活性 1 (%)	マクロファージ活性 2 (%)
第1群	組成物 1	250mg/kg	117 ± 28	209	189
第2群	組成物 1	500mg/kg	389 ± 57	695	627
第3群	組成物 2	250mg/kg	118 ± 30	211	190
第4群	組成物 2	500mg/kg	156 ± 27	279	252
第5群	—	—	56 ± 10	100	—
第6群	—	—	62 ± 7	—	100

[0023]As compared with the 5th group and the 6th group, the number of macrophages increased both the 1st group - the 4th group, and macrophage activity was accepted. Especially this effect was remarkable in the 2nd group.

[0024]One groups [ten] divided the 60 same mice as the example 2 of the macrophage activity grant effect examination of example of examination 4 GLE, or ABME into each six groups, the cancer cell was transplanted like [group / 11th] the example 2 of an examination from the 7th group, and administration of GLE, ABME, or a physiological saline was performed. The 12th group did not transplant a cancer cell and prescribed only the physiological saline for the patient. Subsequently, the macrophage activity 1 and 2 as well as the example 3 of an examination was computed. A result is shown in Table 4.

[0025]

[Table 4]

試験群	投与物	1回の投与量	マクロファージ数 ($\times 10^3$)	マクロファージ活性 1 (%)	マクロファージ活性 2 (%)
第7群	GLE	62.5mg/kg	90 ± 17	149	121
第8群	GLE	125mg/kg	98 ± 22	209	169
第9群	ABME	187.5mg/kg	119 ± 36	253	205
第10群	ABME	375mg/kg	133 ± 41	283	229
第11群	—	—	47 ± 10	100	—
第12群	—	—	58 ± 13	—	100

[0026]The number of macrophages and the macrophage activity 1 and 2 were inferior to the 1st group, the 2nd group, and the 4th group in the 7th group, the 8th group, and the 10th group. The

combined effect of GLE, ABME, and RJ was checked from the examples 3 and 4 of an examination.

[0027]

[Effect of the Invention]According to this invention, drugs and functional food excellent in the anticancer operation or the macrophage active work can be provided. Since the extract and royal jelly of what was especially conventionally used as foods by this invention are considered as a formed part, there are no side effects.

Therefore, the administration and ingestion over a long period of time are possible.

[Translation done.]